Clinical Observations from the PSRT

Regional Meeting

October 4, 2010

Outline

- BV Testing
- Proteinuria
- Hematuria

BV

BV Blue Testing at Screening

Site	% of BV tests at screening per enrollments	% of BV tests Positive	% of KOH tests at screening per enrollments	% of KOH tests Positive
a	2.2	0	0	NA
b	4.5	0	7.6	40
c	2.7	33	3.6	0
d	0	NA	0	NA
e	**17.1**	17	**20**	14
f	7.4	11	3.3	75
g	2	0	2.9	33
h	8	27	8.7	25
i	**19.1**	18	**20.2**	6
j	3.3	0	3.3	0
k	2.4	75	3.6	17
l	**15.2**	31	**21**	27
m	**52.2**	24	**15**	29
n	7.1	0	0	NA
o	8.8	0	0	NA
	10.4	**22**	**7.5**	**23**

Accounting for the Difference

- Women at some sites have more BV than other sites?
- Differential reporting of symptoms by participants per site?
- Differential appreciation of abnormal pelvic exam or participant symptoms by clinicians per site?

Are Microflora of Women Different Between Sites?

Site	% of BV tests at baseline per enrollments	% of BV tests Positive	% of KOH tests at baseline per enrollments	% of KOH tests Positive	BV by Nugent Score-SAMPLING
a	2.2	0	0	NA	38 (34%)
b	4.5	0	7.6	40	1(11%)
c	2.7	33	3.6	0	11 (25%)
d	0	NA	0	NA	
e	**17.1**	17	**20**	14	
f	7.4	11	3.3	75	12 (39%)
g	2	0	2.9	33	31 (30%)
h	8	27	8.7	25	34 (43%)
i	**19.1**	18	**20.2**	6	1 (25%)
j	3.3	0	3.3	0	25 (30%)
k	2.4	75	3.6	17	57 (42%)
l	**15.2**	31	**21**	27	18 (38%)
m	**52.2**	24	**15**	29	12 (43%)
n	7.1	0	0	NA	
o	8.8	0	0	NA	
	10.4	**22**	**7.5**	**23**	

BV Testing in Follow-Up

- 100 BV blue tests performed
  - 5 at enrollment visit
  - 9 at scheduled pelvic exam visit (month 6)
  - 86 at non scheduled pelvic exam visits
    (interim or non-semiannual visits)
- Suggests BV tests are largely being performed based on participant report

BV Testing at Enrollment vs Follow-Up

site	% of BV tests at baseline per enrollments	% BV test in follow-up per enrollment	% tests for BV tests in follow-up with no PE or AE
a	2.2	11.22	9.10
b	4.5	5.95	0.00
c	2.7	11.18	17.60
d	0	5.00	0.00
e	**17.1**	1.79	0.00
f	7.4	6.43	0.00
g	2	5.50	33.30
h	8	4.86	0.00
i	**19.1**	4.50	14.30
j	3.3	9.57	33.30
k	2.4	1.11	0.00
l	**15.2**	4.93	14.30
m	**52.2**	13.18	0.00
n	7.1	0.00	0.00
0	8.8	0.00	0.00

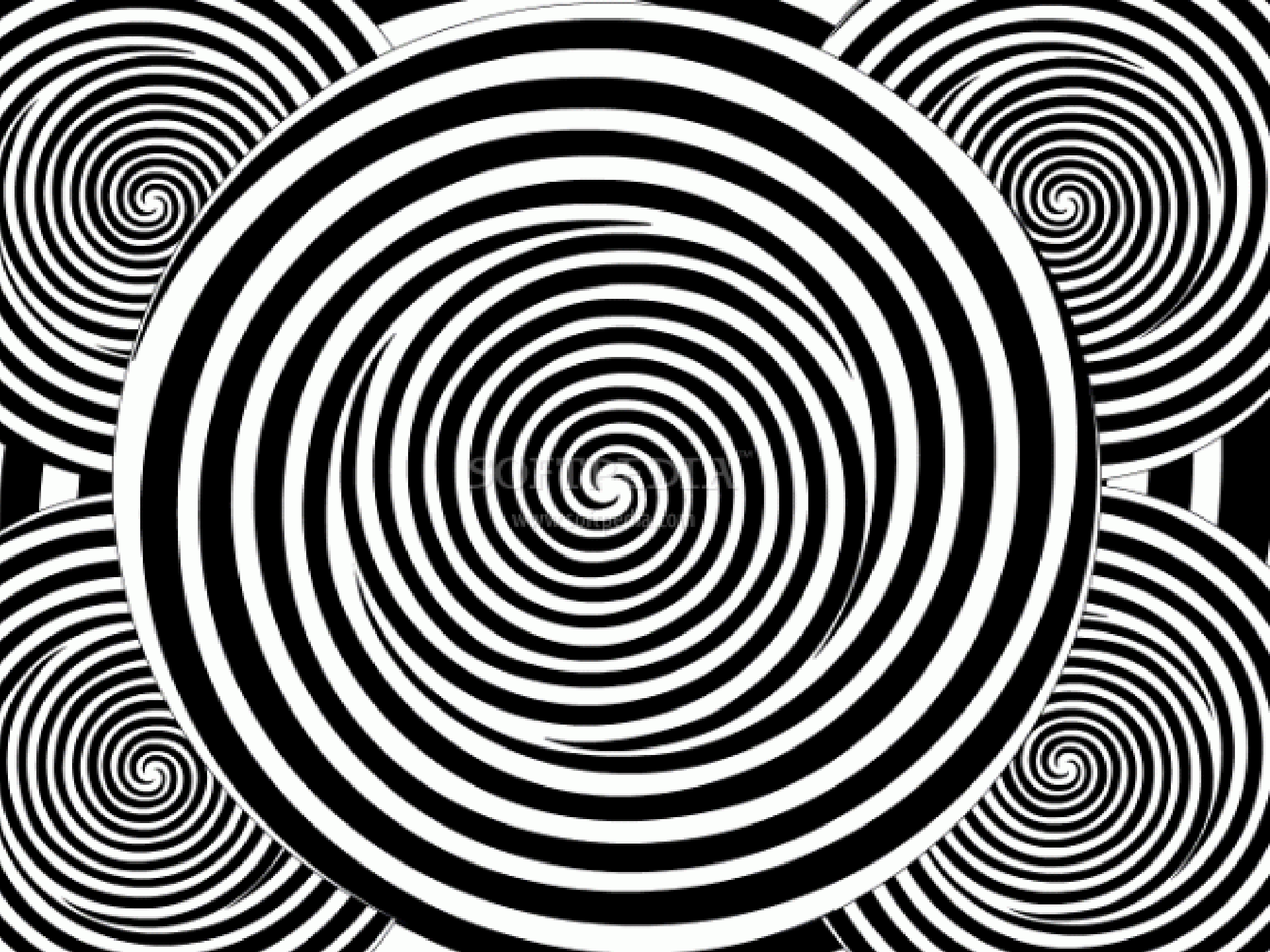
When do You Test for BV?

- When participant is symptomatic?
- When the clinician notices a discharge?
- Are there other situations in which you might test?
  - Suspect cervicitis based on exam?
  - Suspect PID based on exam?

Trying to Understand Trends

- Why would there be more BV testing in the screening process than in follow-up?
  - Is more likely to be clinician driven at baseline and participant driven in follow-up?
  - Do you approach BV testing differently at screening than you do in follow-up?

Proteinuria

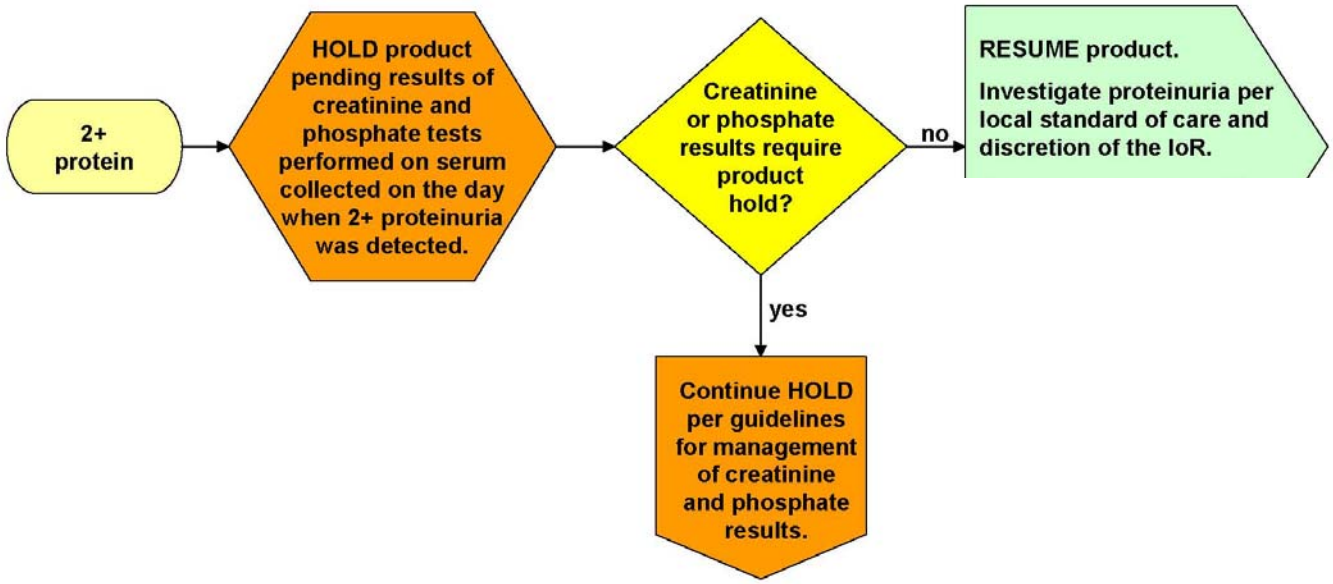


Proteinuria- Case One

- Participant was randomized to the oral arm
- At Month 3 visit she had a 2+ proteinuria, positive leucocytes (+), negative nitrites and had no urinary symptoms.

SSP Section 10

VOICE Product Use Management: Proteinuria 2+
ORAL Study Product



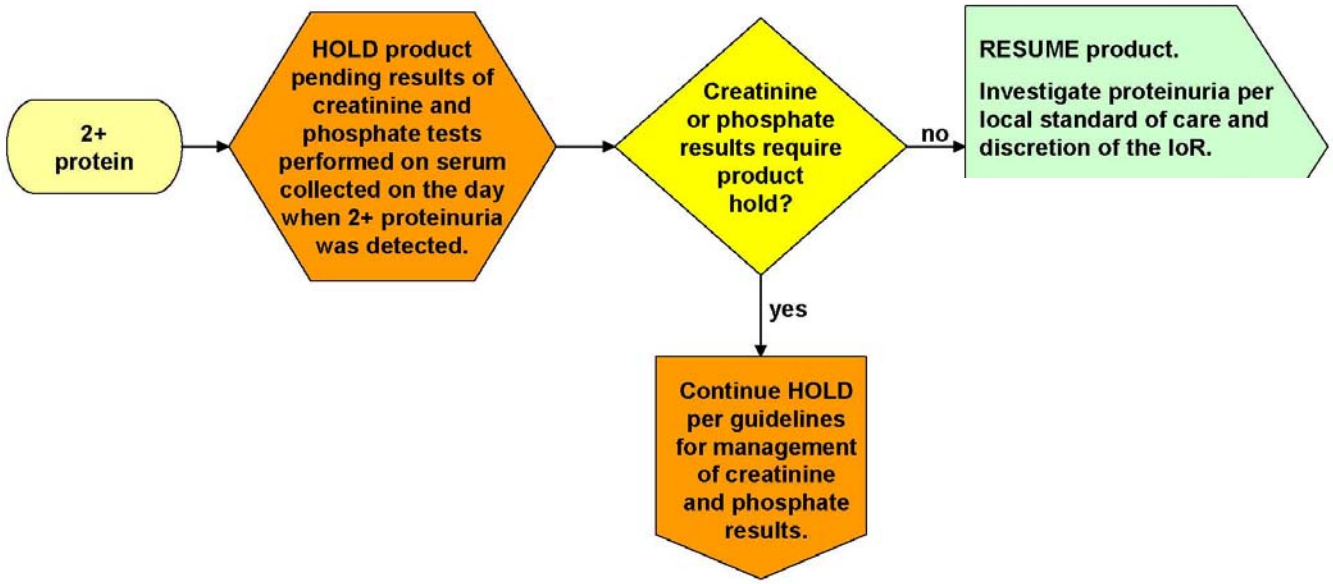
Protocol Reference: Section 9.6

Case One

- Q: Would you hold product?
  - YES. Until serum chemistries returned normal
- Chemistries are normal.
- Q: Do you need to recheck protein before restarting product?

SSP Section 10

VOICE Product Use Management: Proteinuria 2+
ORAL Study Product



Protocol Reference: Section 9.6

Case One

- Q: When will you check urine dip again?
  a. At next scheduled monthly visit or sooner if clinically indicated
  b. In 1-2 weeks, to document resolution of proteinuria
  c. At next protocol specified check- month 6

Proteinuria Case One

- Barring clinical indication to check sooner, recheck at the next monthly visit.
- SSP 11.11.1
  - Study staff also must follow all AEs to resolution or stabilization. As a general operational guideline, “resolution” is defined as returning to the condition or severity grade that was present at baseline (i.e., at the time of randomization) and “stabilize” is defined as persistence at a certain severity grade (above baseline) for three consecutive monthly evaluations.

Take Home Message

- No need to recheck an abnormal lab value prior to the next monthly visit unless specified in the protocol or by the PSRT

OR

UNLESS CLINICALLY INDICATED!

Proteinuria: Case One Continued

- The same participant returns for her Month 4 visit. You check a urine dipstick as per the SSP instructions to document resolution or stabilization.
- No guidance in protocol or SSP regarding what to do with these results.
- PSRT recommendations

Proteinuria: Case One

- Suppose, the dipstick shows no proteinuria

- When will you check urine dipstick again?
  - In 1-2 weeks
  - At the next monthly visit (month 5)
  - At the next protocol specified check (month 6)

Proteinuria: Case One

- Suppose, the dipstick shows no proteinuria
- When will you check urine dipstick again?
  - In 1-2 weeks
  - At the next monthly visit (month 5)
  - At the next protocol specified check (month 6)
- You have documented resolution as per SSP 11.1.1

Proteinuria: Case One

- Suppose the dipstick shows 1+ proteinuria

- When will you check urine dipstick again?
  - In 1-2 weeks
  - At the next monthly visit (month 5)
  - At the next protocol specified check (month 6)

Proteinuria: Case One

- Suppose the dipstick shows 1+ proteinuria
- When will you check urine dipstick again?
  - In 1-2 weeks
  - At the next monthly visit (month 5)
  - At the next protocol specified check (month 6)
- You need to document stabilization over 3 months or resolution to baseline

Proteinuria: Case One

- Suppose the dipstick shows 2+proteinuria
- Do you hold product?
- Do you send chemistries again?
- When will you check urine dipstick again?
  - In 1-2 weeks
  - At the next monthly visit (month 5)
  - At the next protocol specified check (month 6)

Proteinuria: Case One

- Suppose the dipstick shows 2+proteinuria
- Do you hold product? YES
- Do you send chemistries again? YES
- When will you check urine dipstick again?
  - In 1-2 weeks
  - At the next monthly visit (month 5)
  - At the next protocol specified check (month 6)

Proteinuria: Case Two

- A participant is randomized to the oral arm.
- At Month 3 visit, she is asymptomatic but is noted to have 1+leukocytes on dipstick.
- A urinalysis and culture is sent to investigate the finding of leukocytes.
- It shows no growth, 1+ protein
- Please comment

Proteinuria: Case Two

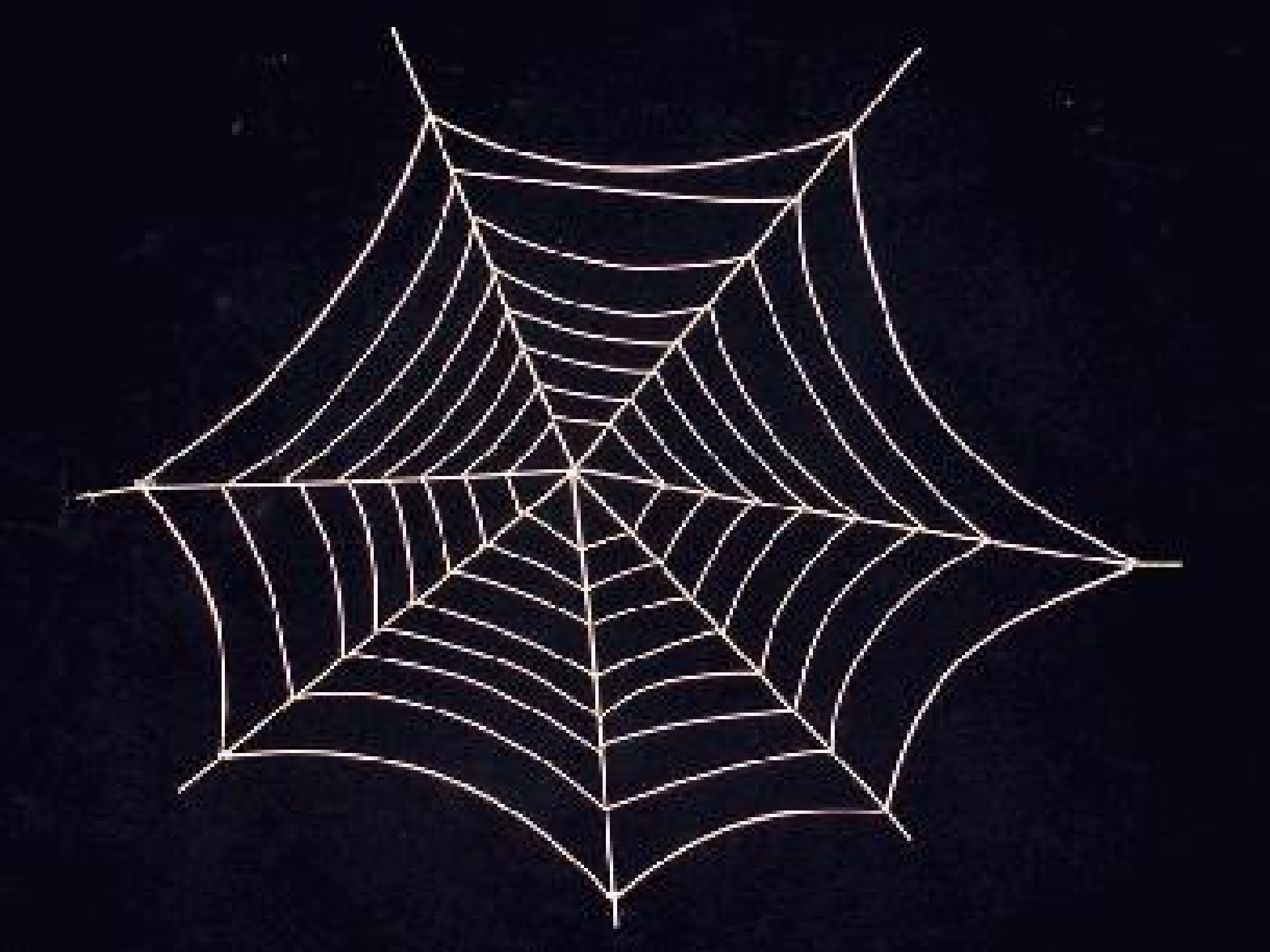
- She returns in 10 days later per protocol for reevaluation of proteinuria.
- Urinalysis is negative
- At the next monthly visit (Month 4), a urine dipstick is checked and is negative for protein
- At the next monthly visit (Month 5), a urine dipstick is checked and shows 1+ proteinuria
- Please comment

Proteinuria

- She returns in 10 days later per protocol for reevaluation of proteinuria.
- She is noted to have 2+proteinuria, product is held, and chemistries sent
- Chemistries are normal
- Participant represents 1 week later and is without complaint. A urine dipstick shows 1+
- Please comment

Take Home Messages

- Low grade proteinuria is common and difficult to interpret
- Restrict urine dipsticks to protocol directed and clinically indicated checks



Hematuria

- 120 AEs for “hematuria”
  - Gross blood in urine per participant report
  - Grass blood in urine per clinician report
  - Dipstick hematuria
  - Microscopy

Hematuria: The Problem

- Some sites use 9 reagent strip; others use 4
- Relying on dipstick for the diagnosis of hematuria is problematic
  - False positive are common
    - Dehydration
    - Exercise
    - Non urologic sources
- Blood detected on dipstick is not on the DAIDS toxicity table. How should they be graded?
- Not all sites have the capacity to confirm positive dipstick with microscopy

Hematuria: Proposition

- Have all sites move towards the 4 reagent strip
  - Is this possible?
- Confirm any blood on dipstick performed for clinical indications with microscopy
- Only confirmed hematuria detected by microscopy will be reported (no dipstick reports)

Thank You!

Site Management: Syndromic Management of STDs

- Which conditions do you treat syndromically?
  - Cervicitis?
  - Vaginal Discharge?
- Do you treat for BV or trichomonas empirically in the setting of syndromic management?

Site Management: Syndromic Management of STDs

- Which conditions do you treat syndromically?
  - Cervicitis?
  - Vaginal Discharge?
- Do you ever treat for BV or trichomonas empirically in the setting of syndromic management or do you rely on the rapid test results?

Questions

AEs for BV Related Symptoms by Site per total AEs

Site	BV	Discharge	Erythema	Itch	Odor	Pain	BV Related
a	1.5	2.2	0	3.0	0.8	1.5	9.0
b	1.8	9.1	0	**9.1**	0	0	20.0
c	0.7	6.4	0	1.4	2.1	2.1	5.7
d	0	17.9	0	3.6	0	3.6	25.0
e	0	14.3	0	**14.3**	0	0	14.3
f	1.7	3.5	0	**8.5**	0	4.5	18.2
g	0	1.3	0	2.6	0	0	3.9
h	1.7	4.0	1.1	2.8	0	0.6	10.2
i	1.0	1.0	0	2.0	0	2.0	6.1
j	1.0	0	0	5.8	0	5.8	12.5
k	1.1	2.7	0	**11.2**	0	2.1	17.0
l	0	7.6	0	**7.6**	0	0	15.1
m	4.0	4.0	0	2.7	0	0	10.7
n	0	0	0	0	0	7.1	7.1
o	0	0	0	0	0	0	0

BV Related AEs by Site per Enrollment

site	BV	Discharge	Erythema	Itch	Odor	Pain	Total
a	2.04%	3.06%	0.00%	4.08%	1.02%	2.04%	12.24%
b	1.19%	5.95%	0.00%	5.95%	0.00%	0.00%	13.10%
c	0.66%	5.92%	0.00%	1.32%	1.97%	1.97%	11.84%
d	0.00%	6.25%	0.00%	1.25%	0.00%	1.25%	8.75%
e	0.00%	1.79%	0.00%	1.79%	0.00%	0.00%	1.79%
f	2.14%	4.29%	0.00%	10.71%	0.00%	5.71%	22.86%
g	0.00%	0.92%	0.00%	1.83%	0.00%	0.00%	2.75%
h	2.08%	4.86%	1.39%	3.47%	0.00%	0.69%	12.50%
i	0.90%	0.90%	0.00%	1.80%	0.00%	1.80%	5.41%
j	1.06%	0.00%	0.00%	6.38%	0.00%	6.38%	13.83%
k	1.11%	2.78%	0.00%	11.67%	0.00%	2.22%	17.78%
l	0.00%	6.34%	0.00%	6.34%	0.00%	0.00%	12.68%
m	4.65%	4.65%	0.00%	3.10%	0.00%	0.00%	12.40%
n	0.00%	0.00%	0.00%	0.00%	0.00%	1.89%	1.89%